

### **REMARKS**

Claims 1-4, 6-12, 18-25 and 27 are pending. The claim are presented in a revised format per the USPTO's announcement 'Amendments in a Revised Format Now Permitted', dated 31 January 2002. Accordingly, a complete listing of all claims that are, or were in the application, along with an appropriate status identifier, is provided above in the section entitled "Amendments to the Claims".

### **PRIORITY**

Applicant respectfully disagrees with the Examiner's assertion that the earlier-filed application does not provide support for claims of the current application. Particularly, Applicant believes that Provisional application 60/181,631 filed 10 February 2000 (hereinafter "'631'"), upon which priority is claimed, provides support under 35 USC. §112 for claims 1-4, 6-12, 18-20, and 23-25 of the present application as follows:

The '631 application teaches a first and second subpopulation of microspheres on page 2, paragraph 5. Specifically, the application states that a number of different samples are loaded onto a slide. The different samples are then processed in parallel. In addition, the title of the application is "Alternative Substrates and Formats for Bead-Based Array of Arrays<sup>TM</sup>." Beads and microspheres are synonymous with regard to this application, as is well known in the art. The disclosure of a number of different samples loaded onto a bead-based array correlates with multiple subpopulations of microspheres, and particularly the claim element of a first and second subpopulation of microspheres. Item 6 of page 2 of the '631 application further enumerates measures that can be taken to separate individual arrays. Such disclosure presupposes the existence of subpopulations that make up the individual arrays. Clearly a first and second subpopulation of microspheres is supported by the '631 application.

The '631 application also provides support for a random distribution of microspheres on a substrate surface. Specifically, the application states that the present invention describes the use of alternative substrates for randomly-assembled Bead Arrays<sup>TM</sup> and Array of Arrays<sup>TM</sup>.

Moreover, the application states that preferred embodiments of the substrate may comprise a plastic or glass format of a microscope slide (page 1, number 4, second and third paragraphs). A randomly assembled array, in the context of this application, necessarily means that microspheres are randomly distributed on the surface of the substrate, because the arrays are "bead-based" (as the title indicates) and assembly requires distribution on the beads on the surface of the substrate.

In contrast to the Examiners position, Applicant submits that the '631 application also teaches a distance between centers of a first and second microsphere subpopulation. Specifically, on the bottom of page 1, the application states that for high resolution scanners ( $<5\mu\text{m}$ ), close spacing ( $<15\mu\text{m}$ ) between bead features can be employed to create extremely high density arrays. For more common lower resolution scanners ( $>5\mu\text{m}$ ), bead spacing could be increased to  $15\text{-}20\mu\text{m}$ . These statements combined with the discussion above regarding first and second microsphere subpopulations makes clear that the '631 application provides proper support for the claims of the present application. Spacing between centers of microspheres is a convenient point of reference for measurement purposes. Moreover, the distance can be computed by back-calculating the dimensions of a slide and dividing by the number of wells (2-4 million).

#### **Claim rejections based under 35 U.S.C. § 102**

Claims 1-4, 6-7, 9-12, 18-20 and 23-25 are rejected under 35 U.S.C. § 102(b) as being anticipated by Brenner (U.S. Patent No. 5,863, 722, issued 26 January 1999). Applicants

respectfully traverse.

Brenner et al. is directed to a method of sorting polynucleotides through the use of oligonucleotide tags by specifically hybridizing the tags attached to the polynucleotides to their complements on solid phase supports. Brenner et al. does not teach a microscope slide including discrete sites where the sites are separated by a distance of less than 50 $\mu$ m, an aspect of claims 1 and 18, from which all other claims depend.

In contrast, claim 1, from which claims 2-12 depend and claim 18, from which claims 19-26 depend are both directed to a microscope slide composition (claim 1) and a method of making a microscope slide composition (claim 18) each comprising a surface with discrete sites, where the sites separated by a distance of less than 50 $\mu$ m, wherein said substrate comprises the dimensions of a microscope slide, a population of microspheres comprising at least a first and second subpopulation, wherein said microspheres are randomly distributed on the surface.

The law is well established that in order to anticipate a claim, the prior art must disclose “each and every element” of the claimed invention *SSIH Equipment S.A. v. U.S. Inc. Int’l. Trade Commission*, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), “[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference.” (Emphasis added). See also *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 33 USPQ2d 1496 (Fed. Cir. 1995).

The Examiner cites to column 10, lines 30-35 and column 20, lines 32-35 of Brenner for the assertion that Brenner teaches sites separated by a distance of less than 50 $\mu$ m. Column 10, lines 30-35 discuss bead size and column 20, lines 32-35 discuss resolving capability of scanning systems. The mere description of bead diameter and scanning system resolution capability in

Brenner et al. does not specifically teach or suggest a substrate having discrete sites separated by a distance of less than 50 $\mu$ m.

Therefore, each and every element is not present in the cited art. As stated above, Brenner does not teach or suggest a microscope slide with discrete sites where the sites are separated by a distance of less than 50 $\mu$ m, an aspect of claims 1 and 18, from which all other claims depend.

Accordingly, the rejection is improper and Applicants respectfully request the withdrawal of the rejection.

Claims 1-3, 6-11, 18-20, 23 and 27 are rejected under 35 U.S.C. § 102(e) as being anticipated by Fan et al. (U.S. Patent No. 2002/0132241 A1, filed 7 February 2000). Applicants respectfully traverse.

The Examiner has incorrectly stated the filing date of Fan et al. to be Feb. 7, 2000, when in fact the filing date is July 24, 2001. In addition, The Examiner has not pointed to where in the Feb 7, 2000 provisional application, from which Fan et al. claims priority, there is support for the assertion that Fan et al. anticipates the claims of the present invention. Therefore the rejection is improper. Accordingly, Applicants respectfully request the withdrawal of the rejection.

**Claim rejections based under 35 U.S.C § 103(a)**

Claims 4, 12, 24 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fan et al. (U.S. Patent Application No. 2002/0132241 A1, filed 7 February 2000) in view of Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999).

For the reasons set forth above, Fan et al. is an improper reference as the Examiner has cited the wrong filing date of Fan et al. and has not shown where in the Feb 7, 2000 disclosure there is support for the claimed invention.

In addition as stated above, Brenner et al. does not teach a microscope slide including discrete sites where the discrete sites are separated by a distance of less than 50µm, an aspect of claims 1 and 18, from which all other claims depend.

Applicant notes that in order to establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all the claim limitations” (MPEP § 2143).

Brenner et al. as previously stated does not teach or suggest a microscope slide including discrete sites where the discrete sites are separated by a distance of less than 50µm. Therefore, the requirement that , the prior art reference (or references when combined) must teach or suggest all the claim limitations has not been met. Accordingly the rejection is improper. Applicants respectfully request the withdrawal of the rejection.

Claims 1-4, 6-12, 18-20 and 23-25 and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Walt et al. (WO 98/40726, published 17 September 1998) in view of Noonan et al. (U.S. Patent No. 6, 129, 896, filed 17 December 1998) and Van Ness et al. (U.S. Patent No. 6,248,521, issued 19 June 2001). Applicants respectfully traverse.

Claims 1 and 18, from which all other claims depend are directed to a microscope slide composition (claim 1) and a method of making a microscope slide composition (claim 18) each comprising a surface with discrete sites, where discrete sites are separated by a distance of less than 50µm, wherein said substrate comprises the dimensions of a microscope slide, a population of microspheres comprising at least a first and second subpopulation, wherein said microspheres are randomly distributed on the surface .

As the Examiner is aware, to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally

available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Vaeck*, 947 F2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Here, there is lacking any motivation to modify or combine references to reach the claims of the present invention. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the glass slide dimensioned substrate of Van Ness et al. to the substrate of Walt et al. and to format the substrate comprising microspheres to the format of a glass slide for the obvious benefits of facility of illumination and detection using a microscope as taught by Van Ness et al. Although the Examiner cites to the abstract in Noonan for the proposition that the individual fibers in Noonan can be formatted to desired dimensions, there is no discussion within the abstract of Noonan about desired dimensions.

In addition, Van Ness et al. does not teach or suggest random distribution of microspheres on the surface of a substrate, where the substrate comprises the dimensions of a microscope slide. In fact, Van Ness teaches away from random distribution of microspheres. See Van Ness et al. column 6, lines 56-60, where there is a discussion of applying nucleic acids to substrates by using a delivery mechanism capable of “positioning” small amounts of liquids in small regions and column 7, lines 19-22 where there is a discussion under the same heading as above, further discussing the inhibition of allowing the sample from randomly dripping or running during transport. A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). The references when combined would not teach or suggest random distribution of microspheres on the surface of a substrate where the substrate comprises the dimensions of a microscope slide in light of the

disclosures in the art that teach away from the claims of the present invention.

In addition, Applicants submit that the Examiner's statement of the motivation to apply the glass slide substrate of Van Ness to the substrate of Walt, expressly taught by Van Ness for the obvious benefits of facility of illumination and detection using a microscope slide does not provide the specific guidance required to provide motivation to modify or combine the references of Van Ness and Walt to reach the claims of the present invention.

"Obvious to try" is not the standard and the very general statement that the Examiner points to in Van Ness et al. that using a microscope for detection for facilitating illumination could apply to any number of methodologies. there is no teaching or suggestion in Van ness for using beads at all, let alone beads on a microscope slide as claimed in the present invention. It is improper to use an obvious to try approach or to cite to only general guidance as to the particular form of the claimed invention or how to achieve it. See *In re O'Farrell*, 853 F. 2d 894,903, 7 USPQ2d 1673,1681 (Fed. Cir. 1988). It is insufficient that the prior art disclosed the components of the patented invention, either separately or used in other combination; there must be some teaching, suggestion, or incentive to make the combination made by the inventor. *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 15 USPQ2d 1321 (Fed. Cir. 1990). The district court did not commit reversible error "by requiring that a claimed invention be "clearly suggested" by the prior art in order to be obvious. *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 16 USPQ2d 1923 (Fed. Cir. 1990).

Applicants submit that there is lacking any suggestion in the references to modify the references or to combine them to reach the claims of the present invention. Therefore, the requirement that there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify

the reference or to combine reference teachings has not been met. Accordingly, the rejection is improper and the Applicants respectfully request the withdrawal of the rejection.

Claims 21 and 22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Walt et al (WO 998/40726, published 17 September 1998) in view of Noonan et al. (U.S. Patent No. 6,129,896, filed 17 December 1998) and Van Ness et al. (U.S. Patent No. 6,248,521, issued 19 June 2001) as applied to Claim 18 above and further in view of Gentalen et al (U.S. Patent No. 6,036,643 B1, filed 24 August 1998). Applicants respectfully traverse.

The disclosures of Walt, Noonan and Van Ness are discussed above and are incorporated at this point by reference.

The Examiner states that gentalen teaches that supopulation ratios are derived based on experimental design. Gentalen does not specifically teach or suggest discrete sites separated by a distance of less than 50 $\mu$ m.

Claims 21 and 22 are dependent from claims 1 and 18. These claims distinguish the cited art for the reasons set forth above. Gentalen does not supply the deficiencies of Walt, Noonan or Van Ness for the foregoing reasons. Accordingly, the rejection is improper and Applicants respectfully request the withdrawal of the rejection.

Claims 21 and 22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brenner (U.S. Patent No. 5,863,722, issued 26 January 1999) in view of Gentalen et al. (U.S. Patent No. 6,306,643 B1, filed 24 August 1998).

Claims 21 and 22 are dependent from claims 1 and 18. These claims distinguish the cited art for the reasons set forth above. Gentalen does not supply the deficiencies of Brenner et al. for the foregoing reasons. Accordingly, the rejection is improper and Applicants respectfully request the withdrawal of the rejection.



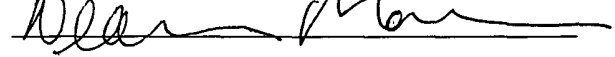
Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

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Respectfully submitted,

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